Reviews/Analyses

Airport malaria: a review

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Cases of malaria occasionally arise among individuals who have never visited a malarious area. Such patients, who also lack a history of blood transfusions or intravenous drug abuse, are usually shown to have "airport malaria". Most reports of airport malaria consist of case histories, although some epidemiological reviews have also appeared. The clinical and epidemiological features of 29 cases of airport malaria that were reported in Europe from 1969 to 1988 are reviewed here. Although airport malaria is rare, the apparent absence of risk factors for the disease in a patient's history can result in delays in diagnosis and appropriate treatment. Tests to exclude malaria should therefore be carried out on patients who work at or live near an international airport and who present with acute febrile illnesses.

Malaria has long been recognized as an important health hazard to travellers who have come from affected areas. Also, the increasing prevalence of drug-resistant strains of *Plasmodium falciparum* has greatly enhanced both the occurrence and the seriousness of malaria in nonimmune individuals. Provided medical practitioners are reasonably well aware of this risk, the possibility of malaria is unlikely to be missed in the great majority of affected travellers. It is therefore fundamental to the recognition of malaria and numerous other travellers' ills that geographical histories of patients be taken.

Much less well recognized, despite its periodic description in the medical literature, is airport malaria. By definition, such malaria is acquired through the bite of an infected tropical anopheline mosquito by persons whose geographical history firmly excludes exposure to this vector in its natural habitat. In such circumstances, diagnosis of malaria can be missed or delayed. Reports on airport malaria have usually concentrated on its epidemiology, while the clinical aspects frequently have not been analysed. In the present review an attempt has therefore been made to provide key clinical information about the condition.

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Clinical and epidemiological data

A summary of data on 29 cases of airport malaria that occurred in Europe from 1969 to 1988 is shown in Table 1. Below are presented additional details on some of these cases.

- Patients 1 and 2, who had malaria in 1969, were described in 1970 by Cartier & Louvet (cited by Gentilini et al. (*1*)) as obscure cases of autochthonous malaria contracted while on holiday in Brittany, on the extreme western Atlantic seaboard of France. Following a reclassification of autochthonous malaria by Gentilini & Danis (*4*), these so-called "Breton cases" were reinvestigated by Doby & Guiguen in 1981 (*2*). The two holiday-makers had become ill 11 days after their arrival from the Paris area, where they lived in a street adjacent to Le Bourget International Airport. It was concluded that they were probably infected by an imported mosquito just before they set off on holiday, and not by a local mosquito while on holiday, as had previously been believed.
- Patient 9 was one of the most intensively investigated cases (*7*). Numerous laboratory and other tests, including several blood counts, failed to reveal the true cause of his illness. He was treated for tuberculosis, until examination of liver biopsy tissue showed changes that were indicative of malaria.
- Patient 15 was a saxophonist who played in the French Republican Guard and was one of two cases of airport malaria reported during winter in Europe

Table 1: **Summary of the clinical and epidemiological data on the 29 published cases of airport malaria covered in the review**

Case number, age (years) and sex	Date of illness	Airport	Country	Distance: home to airport (km)	Occupation (at or near airport)	Length of illness (days)	
						On admission to hospital	Before diagnosis
1 31 F	August 1969	Le Bourget	France	0.5	—	—	—
2 Adult M	August 1969	Le Bourget	France	0.5	—	2	—
3 Adult M	August 1970	Zurich	Switzerland	—	Soldier	—	7
4 Adult M	August 1970	Zurich	Switzerland	—	Soldier	—	7
5 60 F	August 1972	Zurich	Switzerland	"close"	—	—	—
6 27 M	October 1974	Orly	France	<2	Ex-prisoner	—	15
7 57 M	July 1976	Charles de Gaulle and Le Bourget	France	—	Caretaker	—	—
8 20 M	August 1976	Charles de Gaulle	France	—	Cargo handler	4	4
9 41 M	August 1976	Charles de Gaulle	France	—	Airport storeman	—	>42
10 76 M	August 1977	Charles de Gaulle	France	1.5	Pensioner	3	—
11 26 M	September 1977	Charles de Gaulle	France	—	Customs officer	—	—
12 Adult M	August 1977	Charles de Gaulle	France	—	Policeman	—	—
13 Adult M	June 1978	Charles de Gaulle and Le Bourget	France	—	Accountant	—	—
14 24 F	August 1978	Schiphol	Netherlands	0.3	—	9	10
15 45 M	February 1978	Charles de Gaulle	France	—	Guard's band saxophonist	—	>7
16 10 F	August 1979	Schiphol	Netherlands	<2	—	—	—
17 18 M	July 1982	Brussels	Belgium	<2	Mechanic	—	>28
18 24 M	August 1982	Brussels	Belgium	<2	Mechanic	6	20
19 27 M	1983	Brussels	Belgium	—	Baggage handler	—	—
20 48 M	July 1983	Gatwick	England	10	Publican	14	14
21 Adult F	August 1983	Gatwick	England	14	Housewife	10	10
22 76 F	August 1984	Madrid	Spain	<6	—	30	>30
23 30 F	July 1985	Ciampino/ Fiumicino	Italy	5 25	—	3	31
24 Adult M	June 1986	Brussels	Belgium	—	Customs officer	—	—
25 Adult M	June 1986	Brussels	Belgium	—	Customs officer	—	—
26 Adult M	June 1986	Brussels	Belgium	—	Customs officer	3	—
27 Adult M	June 1986	Brussels	Belgium	—	Customs officer	—	—
28 Adult M	June 1986	Brussels	Belgium	—	Customs officer	—	—
29 67 F	December 1988	—	Italy	—	—	14	21

[a] A = anaemia; C = chills; D = diarrhoea; Fe = fever; H = headache; He = hepatomegaly; Hesp = hepatosplenomegaly; J = jaundice;

Leukocyte count ($\times 10^9$/l)	Platelet count ($\times 10^9$/l)	Parasitaemia	Clinical features[a]	Outcome: C=cured D=died	Epidemiological comments	Reference
—	—	—	Fe, N	C	Cases 1 and 2 were close friends and lived in the same street	(1,2)
—	—	—	Fe, coma. Malaria diagnosed at autopsy	D		
—	—	—	Fe, H, Ma, Hesp	C	Cases 3 and 4 were stationed on a military base near the airport	(3)
—	—	—	Fe, H, Ma, Hesp	C		
—	—	—	Infected with *P. malariae*	—	—	(3)
6.6	—	Numerous	Fe, C, H, MC	C	Village virtually enclosed by the Orly runways	(1,4)
—	—	—	Fe, J	—	Lived ca. 6 km from airport	(1,4)
4.0	—	5%	Fe, H, C, V, dry cough, hypotension	C	Were cases 8 and 9, who had onset of illness 2 weeks apart, bitten by the same mosquito?	(5–7)
4.7	340	Numerous	Fe, C, A, J, He, treated for tuberculosis; malaria then suspected on liver biopsy	C		
12.0	—	23%	Fe, C, D, V, cough, abdominal pain, dehydrated, schizonts	D	Were cases 10 and 11, who had onset of illness within 1 week, bitten by the same mosquito?	(5,6,8)
—	34	—	Fe, J, RF, Hesp, circulatory collapse, coagulopathy	C		
—	—	—	Infected with *P. vixax*		—	(4,9)
—	—	—	—	—	Lived between Charles de Gaulle and Le Bourget	(4)
8.4	74	5%	Fe, A, RF. Treated for Gram-negative sepsis	C	—	(10)
—	—	Scanty	Recurrent D, followed 2 days later by Fe, C, and H	C	—	(11)
—	—	—	—	—	Lived in Amsterdam but stayed near airport about 4 weeks before onset of illness	(10)
Normal	85	Numerous	Fe, H, C, Sp. Gametocytes present	C	Cases 17 and 18 were brothers who did not work at airport; probably bitten by same mosquito	(12)
21.5	40	Numerous	Fe, H, C, J, A, RF, coma, Hesp, gametocytes.	C		
—	—	—	—	C	—	(13)
4.4	—	Numerous	Fe, H, C, D, V, He. Treated with erythromycin	C	Public house was popular with aircrews	(14)
2.6	—	Present	Influenza-like illness, D, J, abdominal pain. GP suspected and confirmed malaria.	C	Husband worked at airport. Wife passed public house 10 days before onset of her illness	(14)
21.4	37	Numerous	Fe, C, J, abdominal and chest pain. Gametocytes present	D	Visited daughter's house near airport at the end of July	(15)
—	—	12 000/μl	Fe, H, C, J, A, Sp. Pregnant	C	—	(16)
—	—	—	—	C	Cases 24–28 all worked in the same freight terminal and became ill within the same week—believed to have been bitten by the same mosquito.	(17)
—	—	—	Diagnosed as cerebral malaria with renal failure	C		
—	—	—	Diagnosed as cerebral malaria	D		
—	—	—	—	C		
—	—	—	—	C		
—	—	Numerous	Fe, H, A, J, coma. Gametocytes	C	Daughter-in-law returned from Senegal 20 days before onset of symptoms	(18)

Ma = malaise; MC = mental confusion; N = nausea; RF = renal failure; Sp = splenomegaly; V = vomiting.

(*11*). It was held probable that he had been bitten by a tropical anopheline mosquito while a member of a welcoming party for visiting VIPs who arrived in Paris on an aircraft from Côte d'Ivoire.

- Patients 17 and 18 were brothers, both mechanics, who lived near to, but did not work at Brussels International Airport (*12*). The elder brother (case 18) was hospitalized in a coma with fever, convulsions, jaundice, Cheyne–Stokes respiration, and renal failure. He underwent haemodialysis and supportive treatment, and within a week improved remarkably; during the following week, however, his anaemia recurred. After this patient had spent 3 weeks in hospital, malaria was diagnosed also in his younger brother (case 17); only then was a thick blood film from the elder brother examined and found to contain numerous *P. falciparum* gametocytes.
- Patients 20 and 21 lived in the vicinity of London Airport (Gatwick) (*14*). Patient 20 was landlord of a public house. When he became ill with fever and abdominal symptoms his doctor could find no localizing signs and treated him with erythromycin. Following an initial improvement, the patient's symptoms recurred and eventually his condition deteriorated. After admission to hospital, a diagnosis of cerebral malaria was considered, despite a negative geographical history, and examination of blood films showed numerous *P. falciparum*. Erythromycin, which has marginal antimalarial efficacy, was thought to have been responsible for the initial transient phases of improvement. The public house was frequented by aircrews from Gatwick and it was assumed that an imported, infected mosquito must have been brought to the public house in a vehicle carrying aircrew from the airport. Patient 21 lived about 15 km south-west of Gatwick. Her husband drove daily to the airport where he worked, but he was not involved with aircraft in active service. Following thorough investigation it was thought that both patients 20 and 21 had probably been bitten by the same mosquito, although it remains unclear precisely how this occurred.
- Patient 22, a 76-year-old woman, had visited her daughter who lived near Madrid International Airport (*15*). Subsequently, the woman developed a febrile illness and respiratory symptoms and was treated for pneumonia; 30 days later she was hospitalized with a presumptive bacteraemia for which she was given penicillin and gentamicin; however, she did not respond and became jaundiced. Blood-film microscopy then revealed *P. falciparum* gametocytes and numerous trophozoites. The woman did not respond to treatment with chloroquine and was given quinine; however, she died a few days later of respiratory complications.

Discussion

Definition of airport malaria

The term "airport malaria" originally may have arisen from an erroneous translation of *paludisme aéroporté*, meaning literally "airborne" malaria, which was used by French workers in the late 1970s to identify a subclass of autochthonous malaria acquired through the bite of a tropical mosquito that had been imported by air (*4*). Autochthonous malaria was first defined as a case of the disease in metropolitan France that had been transmitted by local or imported mosquitos, but excluded imported malaria in the form of human cases or carriers, transfusion malaria, accidental malaria, and congenitally acquired cases. Persons who become infected during brief stop-overs at airports in areas that are endemic for malaria or persons who are bitten in-flight by infected mosquitos therefore do not meet the case definition.

Clinical aspects

Although most reports of airport malaria have supplied clinical information, emphasis has generally focused on the epidemiological aspects.

For all the cases reviewed, other routes of infection such as blood transfusion, shared needle transmission, prior exposure in endemic regions, and transmission by local mosquitos had been excluded.

Table 1 shows some of the relevant clinical and epidemiological features of the cases reviewed.

The length of illness before patients were admitted to hospital ranged from 2 days to 30 days, with a median of 6 days ($n = 11$). The length of illness before malaria was diagnosed ranged from 4 days to more than 6 weeks, with a median of more than 14 days ($n = 14$). *P. falciparum* was responsible for 93% of the infections.

By the time parasites were first detected in samples of blood from the patients, gametocytes were present in four (31%) of 13 cases of falciparum malaria for which parasitological data were published. All four patients had been ill for 3 weeks or longer.

Quantitative parasitaemic data were reported for only 12 cases. A parasitaemia of 23% occurred in a 76-year-old man with a 3-day history of illness who also had occasional schizonts, and who died on the day after admission to hospital (case 10). Peripheral blood schizonts are rare in cases of falciparum malaria and indicate a poor prognosis. White blood cell counts ranged from 2.6×10^9 per litre to 21.5×10^9 per litre, with 70% being normal or below normal ($n = 10$).

For 21 patients it was established that at least

two-thirds had severe or complicated malaria by the time the cause of their illness was diagnosed. Among the complications were cerebral malaria (6 patients), jaundice (8 patients), anaemia (5 patients), and renal failure (4 patients). One patient clearly had a coagulopathy, as shown by a full coagulation profile, but of six patients for whom platelet counts were available only one was normal and five (83%) had low platelet counts ranging from 34×10^9 per litre to 85×10^9 per litre. The outcome of illness was recorded for 24 patients for whom the case fatality rate was 16.7%.

Parasites were rarely detected during the course of routine haematological investigations, unless microscopy for malaria parasites was specifically carried out. The widespread use of automation in haematology laboratories may be an important factor that contributed to the failure to detect the parasites. Before automation was generally available, malaria parasites were usually detected during routine microscopy of thin blood smears for differential white cell counts. Modern, automated haematology equipment, which can perform both total and differential blood counts, is, however, not designed to recognize malaria parasites. Similarly, thrombocytopenia may not be recognized. Leukopenia and thrombocytopenia are characteristic of falciparum malaria (*19*) and should be used as absolute criteria that indicate a need for urgent investigation for malaria among patients who present with an acute febrile illness.

Epidemiological aspects

The published data on airport malaria reviewed here probably represent the more serious cases that occurred in Europe from 1969 to 1988. Data on mild cases may either not have been considered worth publishing or the patients involved recovered spontaneously without having been diagnosed as having had malaria. Alternatively, serious or even fatal cases of airport malaria may have been misdiagnosed. The true incidence of the condition and the true case fatality rate cannot therefore be established accurately. Of interest is its geographical distribution, all reported cases having occurred in Europe. This may reflect the greater frequency with which European airlines serve Africa. However, although malarious regions of Asia and South America are well served by non-European airlines, airport malaria has not been reported from malaria-free areas in, for example, North America or Japan. Possibly, airline disinsection procedures are more effective in some countries than in others, but this aspect requires further investigation.

Entomological aspects

The potential danger of disseminating the mosquito vectors of malaria and yellow fever by means of aircraft was first recognized more than 50 years ago. In 1986, searches of 27 aircraft from six airlines that had arrived at Nairobi Airport yielded some 150 adult mosquitos, including some *Anopheles gambiae*. Highton & van Someren (*20*) have suggested that mosquitos enter aircraft while they stand at night in open hangars under artificial lights for routine maintenance. Other workers have proposed that, especially during nocturnal stop-overs, the light and warmth of the open passenger cabin and the carbon dioxide emitted by jet engines attract female mosquitos in search of a blood meal (*4, 21*). This is important in view of the frequent requirement, especially in Africa, that passengers remain aboard during brief refuelling stops.

Modern disinsection procedures have not yet eliminated the risk of transporting vectors of exotic diseases, as indicated by the 967 arthropods collected from 592 aircraft that landed at Piarco International Airport, Trinidad, West Indies (*22*). Live mosquitos were also detected in 12 of 67 aircraft that arrived at London Airport (Gatwick). Some of these mosquitos were resistant to organophosphate insecticides and, in addition to disseminating disease, the genes that code for insecticide resistance could be disseminated worldwide in this way (*23*).

In trials carried out by Russell (*24*) on insects that were carried in small cages attached to the internal walls of the inner wheel bays of Boeing 747B aircraft, more than 80% of culicine mosquitos survived in each of six flights that lasted from about 1.5 hours to more than 9 hours. Whereas the external temperature varied between $-47\,^{\circ}C$ and $-54\,^{\circ}C$ at cruising altitude, in the wheel bays the temperature was as high as $28\,^{\circ}C$ and never fell below $8\,^{\circ}C$. Wheel bays are non-pressurized, but the extremely low atmospheric pressures at the aircraft cruising altitudes did not affect most of the insects studied. Russell suggested that, in addition to the cabins and the cargo hold, disinsection of the wheel bays should therefore be considered.

Once a mosquito arrives at an airport, how far can it travel? In some cases of airport malaria, the mosquito, after disembarking, may have been further transported in a motor vehicle (*14*). However, in view of the short distances involved in most cases of airport malaria, the responsible vectors may often have continued their travel unassisted. Even in temperate climates this is feasible during periods of the year when climatic conditions are favourable. With few exceptions, most cases of airport malaria occurred from late June to September, i.e., during the

warmest part of the year in Europe. Active dispersal of *A. gambiae* can be as much as 7 km under favourable wind conditions.[a] When temperature and humidity are favourable, as is often the case during the height of the European summer, imported tropical mosquitos can not only remain alive but also move around considerably. Fertilized female anophelines will then attempt to obtain periodic blood meals, which are essential for the maturation of successive batches of ova. If disturbed while feeding, such mosquitos may bite several hosts to obtain the required amount of blood.

Vector control in aircraft and at international airports

Various methods have been used for the disinsection of aircraft, but the "blocks away" method is still most favoured. This involves manual aerosol application of a specified insecticide to the passenger cabin "and all other accessible interior spaces of the aircraft, except the flight deck" after embarkation of passengers and closure of the doors, but before take-off; the flight deck is treated separately (*25*). Empty aerosol cans must be produced on arrival as evidence of disinsection.

Airlines are responsible for vector control on their aircraft, but the airport health authority must keep the area within the airport perimeter free of the vectors of diseases of epidemiological significance to international health, and must prevent disease vectors from gaining access to aircraft (*26*).

The number of air travellers now exceeds 1000 million annually (*21*) and in that context airport malaria is an unusual event. It has been suggested by Delemarre & van der Kaay that apart from asking "Where have you been and when?" the question "Where do you live?" should also be posed when patients are interviewed (*10*).

Résumé

Le paludisme aéroporté: une mise au point

Depuis plus de 20 ans, on signale régulièrement en Europe occidentale des cas de paludisme aéroporté. Le présent article passe en revue 29 cas qui sont examinés des points de vue épidémiologique et clinique. La plupart sont survenus en plein été, c'est-à-dire dans des conditions climatiques favorables à la survie des moustiques tropicaux. La majorité des patients vivaient à proximité d'un aéroport assurant des liaisons avec des régions d'endémie palustre ou travaillaient dans un tel aéroport ou dans ses environs immédiats, et plusieurs d'entre eux étaient appelés à manipuler le fret ou les bagages, soit comme porteurs, soit comme douaniers. Tous étaient atteints de paludisme à *Plasmodium falciparum*, sauf deux chez lesquels on a identifié *P. malariae* et *P. vivax*, respectivement. Sur les douze patients pour lesquels on dispose de données quantitatives concernant la parasitémie, un seul a été déclaré faiblement infesté; pour les autres, les parasites sanguins ont été qualifiés de "nombreux", ou bien la parasitémie, exprimée par le pourcentage d'érythrocytes infestés, se situait entre 5% et 23%. Des gamétocytes étaient présents chez quatre patients sur treize au moment où les plasmodies ont été détectées pour la première fois dans le sang. En outre, un frottis de sang périphérique a montré la présence de schizontes chez l'un des quatre patients qui sont décédés, un homme de 76 ans dont 23% des érythrocytes étaient parasités. Onze patients étaient malades depuis deux à trente jours (valeur médiane: six jours) lorsqu'ils ont été admis à l'hôpital, et dans quatorze cas, il s'est écoulé de quatre jours à plus de six semaines (médiane: 14 jours) entre le début de la maladie et son diagnostic. Dans un cas, le diagnostic a été porté à l'autopsie, et dans un autre à la suite d'une biopsie du foie. Soixante-dix pour cent des numérations leucocytaires étaient normales ou inférieures à la normale, et la numération plaquettaire pratiquée chez six patients a révélé une thrombopénie dans tous les cas sauf in complica-21 patients, les deux tiers souffraient de complications au moment où le paludisme a été diagnostiqué; il s'agissait de paludisme cérébral (six patients), d'insuffisance rénale (quatre patients), d'ictère (huit patients), d'anémie (cinq patients) et de coagulopathie (un patient). Le taux global de létalité a été de 16,7%.

Il convient de noter que la plupart des appareils automatiques utilisés pour la numération sanguine ne sont pas conçus pour reconnaître les plasmodies; la recherche du paludisme doit donc être explicitement demandée pour tout patient atteint d'une maladie fébrile, surtout si le nombre des leucocytes et des plaquettes est inférieur à la normale. Le fait qu'un malade réside ou travaille à proximité d'un aéroport international doit faire

[a] **Zahar, A. R.** *Vector bionomics in the epidemiology and control of malaria. Part I. The WHO African Region and the southern WHO Eastern Mediterranean Region. Section III: Vector bionomics, malaria epidemiology and control by geographical areas* (*a*) *West Africa*, WHO unpublished document VBC/85.1. (*b*) *Equatorial Africa*, (*c*) *Southern Africa*, WHO unpublished document VBC/85.2. (*d*) *East Africa*, (*e*) *Eastern outer islands*, (*f*) *south-western Arabia*, WHO unpublished document VBC/85.3.

penser au paludisme. Pendant les escales, surtout en Afrique, il est maintenant fréquent que les passagers soient obligés de rester à bord de l'avion, portes ouvertes et lumières allumées. Dans ces conditions, les moustiques sont attirés à l'intérieur de l'avion et les passagers risquent davantage d'être piqués par des insectes infestés que s'ils se trouvaient dans une salle de transit climatisée.

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